

RESEARCH ARTICLE

Genetic modules for α -factor pheromone controlled growth regulation of *Saccharomyces cerevisiae*

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Funding information

Europäischer Sozialfond (ESF) and the Free State of Saxony within the KoSyn project with the SAB grant number, Grant/Award Number: 100382367

Abstract

Saccharomyces cerevisiae is a commonly used microorganism in the biotechnological industry. For the industrial heterologous production of compounds, it is of great advantage to work with growth-controllable yeast strains. In our work, we utilized the natural pheromone system of *S. cerevisiae* and generated a set of different strains possessing an α -pheromone controllable growth behavior. Naturally, the α -factor pheromone is involved in communication between haploid *S. cerevisiae* cells. Perception of the pheromone initiates several cellular changes, enabling the cells to prepare for an upcoming mating event. We exploited this natural pheromone response system and developed two different plasmid-based modules, in which the target genes, *MET15* and *FAR1*, are under control of the α -factor sensitive *PTG1* promoter for a controlled expression in *S. cerevisiae*. Whereas expression of *MET15* led to a growth induction, *FAR1* expression inhibited growth. The utilization of low copy number or high copy number plasmids for target gene expression and different concentrations of α -factor allow a finely adjustable control of yeast growth rate.

KEYWORDS

growth regulation, pheromone response, *Saccharomyces cerevisiae*, synthetic biology, α -factor

1 | INTRODUCTION

Due to the easy genetic tractability and the extensive knowledge regarding its metabolism, genetics and lifestyle, the yeast *Saccharomyces cerevisiae* is a commonly applied microorganism in the biotechnological industry, for example, for beverage, food or biofuel production [1–3]. For

maintaining stability in biotechnological production cultures or co-cultures, one critical point is the controllable growth behavior of the microorganisms. In general, yeast growth can be controlled by the availability of nutrients such as sugars, amino acids, or nitrogen compounds, as these determine development programs and growth rates [4]. Different compounds such as farnesol [5], proteinogenic amino acids as well as the nonproteinogenic amino acids citrulline and ornithine [6], or weak acids like acetic acid or formic acid [7] possess growth-inhibiting effects at high levels. For some applications, the use of specific mutations may also be an alternative constitutive

Abbreviations: GPCR, protein-coupled receptor; HA₃, three copies of the viral hemagglutinin protein tag; Mw calc., calculated molecular weight; RLU, relative nephelometric units; *S. cerevisiae*, *Saccharomyces cerevisiae*.

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The Pheromone Factor

Thomas Stütze



The Pheromone Factor:

Ant Colony Optimization and Constraint Programming Christine Solnon, 2013-03-04 Ant colony optimization is a metaheuristic which has been successfully applied to a wide range of combinatorial optimization problems The author describes this metaheuristic and studies its efficiency for solving some hard combinatorial problems with a specific focus on constraint programming The text is organized into three parts The first part introduces constraint programming which provides high level features to declaratively model problems by means of constraints It describes the main existing approaches for solving constraint satisfaction problems including complete tree search approaches and metaheuristics and shows how they can be integrated within constraint programming languages The second part describes the ant colony optimization metaheuristic and illustrates its capabilities on different constraint satisfaction problems The third part shows how the ant colony may be integrated within a constraint programming language thus combining the expressive power of constraint programming languages to describe problems in a declarative way and the solving power of ant colony optimization to efficiently solve these problems

Learning and Intelligent Optimization: Designing, Implementing and Analyzing Effective Heuristics Thomas Stützle, 2009-11-27 LION 3 the Third International Conference on Learning and Intelligent Optimization was held during January 14 18 in Trento Italy The LION series of conferences provides a platform for researchers who are interested in the intersection of efficient optimization techniques and learning It is aimed at exploring the boundaries and uncharted territories between machine learning artificial intelligence mathematical programming and algorithms for hard optimization problems The considerable interest in the topics covered by LION was reflected by the overwhelming number of 86 submissions which almost doubled the 48 submissions received for LION's second edition in December 2007 As in the first two editions the submissions to LION 3 could be in three formats a original novel and unpublished work for publication in the post conference proceedings b extended abstracts of work in progress or a position statement and c recently submitted or published journal articles for oral presentations The 86 submissions received include 72 ten and four articles for categories a b and c respectively

Advances in Mechatronics and Control Engineering III Prasad Yarlagadda, 2014-10-08 Selected peer reviewed papers from the 2014 3rd International Conference on Mechatronics and Control Engineering ICMCE 2014 August 27 28 2014 Zhuhai China

Ant Colony Optimization and Swarm Intelligence Marco Dorigo, Mauro Birattari, Christian Blum, Maurice Clerc, Thomas Stützle, Alan Winfield, 2008-09-10 The series of biannual international conferences ANTS International Conference on Ant Colony Optimization and Swarm Intelligence now in its sixth edition was started ten years ago with the organization of ANTS 98 As some readers might recall the first edition of ANTS was titled ANTS 98 From Ant Colonies to Artificial Ants First International Workshop on Ant Colony Optimization In fact at that time the focus was mainly on ant colony optimization ACO the first swarm intelligence algorithm to go beyond a pure scientific interest and to enter the realm of real world applications Interestingly in the ten years after the first

edition there has been a growing interest not only for ACO but for a number of other studies that belong more generally to the area of swarm intelligence. The rapid growth of the swarm intelligence field is attested by a number of indicators. First the number of submissions and participants to the ANTS conferences has steadily increased over the years. Second a number of international conferences in computational intelligence and related disciplines organize workshops on subjects such as swarm intelligence and algorithms and colony optimization and particle swarm optimization. Third IEEE started organizing in 2003 the IEEE Swarm Intelligence Symposium in order to maintain unity in this growing field we are currently establishing a cooperation agreement between IEEE SIS and ANTS so as to have 1 IEEE SIS in odd years and ANTS in even years. Last the Swarm Intelligence journal was born.

MEDINFO 2019: Health and Wellbeing e-Networks for All Lucila Ohno-Machado, 2019-11-15. Combining and integrating cross institutional data remains a challenge for both researchers and those involved in patient care. Patient generated data can contribute precious information to healthcare professionals by enabling monitoring under normal life conditions and also helping patients play a more active role in their own care. This book presents the proceedings of MEDINFO 2019 the 17th World Congress on Medical and Health Informatics held in Lyon France from 25 to 30 August 2019. The theme of this year's conference was Health and Wellbeing E Networks for All stressing the increasing importance of networks in healthcare on the one hand and the patient centered perspective on the other. Over 1100 manuscripts were submitted to the conference and after a thorough review process by at least three reviewers and assessment by a scientific program committee member 285 papers and 296 posters were accepted together with 47 podium abstracts 7 demonstrations 45 panels 21 workshops and 9 tutorials. All accepted paper and poster contributions are included in these proceedings. The papers are grouped under four thematic tracks interpreting health and biomedical data supporting care delivery enabling precision medicine and public health and the human element in medical informatics. The posters are divided into the same four groups. The book presents an overview of state of the art informatics projects from multiple regions of the world it will be of interest to anyone working in the field of medical informatics.

Characterization of the Primary Interaction Between the Mating Pheromone, Alpha-factor, and Its Receptor in *Saccharomyces Cerevisiae* Susan Kay Raths, 1987. *Engineering Tuneable Gene Circuits in Yeast* Stephen Checkley, 2015-09-14. Doctoral Thesis Dissertation from the year 2011 in the subject Chemistry Bio chemistry grade pass University of Manchester Manchester Institute of Biotechnology course Systems biology doctoral training program synthetic biology language English abstract. Synthetic biology is an emergent field incorporating aspects of computer science molecular biology based methodologies in a systems biology context taking naturally occurring cellular systems pathways and molecules and selectively engineering them for the generation of novel or beneficial synthetic behaviour. This study described the construction of a novel synthetic gene circuit with interchangeable gene expression components enabling the investigation of tuning circuits for optimal signal to noise ratio. The circuit utilises the inducible downstream transcriptional

activation properties of the pheromone response pathway in the budding yeast *Saccharomyces cerevisiae* as the basis for initiation **Signal Transduction in the Pheromone Response Pathway of *Saccharomyces Cerevisiae*** Aaron M. Neiman,1994 **Mechanical Engineering, Materials and Energy** Grace Chang,2011-12-22 Selected peer reviewed papers from the 2011 International Conference on Mechanical Engineering Materials and Energy ICMEME 2011 October 19 21 2011 Dalian China **Pheromones** Martin C. Birch,1974 *The Synthesis, Biological Activity, and Membrane Binding Properties of Fluorescent Yeast Pheromones and the Partial Purification of the Pheromone Receptor* Christopher B. Sherrill,1995 **Bulletin** ,1908 **Genetic Analysis of the Receptor for the Yeast Pheromone Alpha-factor** Anne Carolyn Burkholder,1986 Endogenous and Exogenous Factors Affecting Pheromone Production and Release in the Omnivorous Leafroller Moth, *Platynota Stultana* (Walsingham) Reginald Paul Webster,1981 **Cold Spring Harbor Symposia on Quantitative Biology** Cold Spring Harbor Laboratory of Quantitative Biology,1933 **Principles and Practice of Constraint Programming** ,2001 Genetic and Functional Analysis of the Yeast Alpha-factor Receptor Johanna Elise Reneke,1989 GENETIC CHARACTERIZATION OF FACTORS INFLUENCING EXPRESSION OF THE CONJUGATION GENES OF THE ENTEROCOCCUS FAECALIS PLASMID PAD1 LINDA TULLY PONTIUS,1991 transcription termination signals seems evident **Proceedings of the National Academy of Sciences of the United States of America** National Academy of Sciences (U.S.),2007 Proceedings of the Genetic and Evolutionary Computation Conference ,2002

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